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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

MAIER, LEIGH C

ART UNIT PAPER NUMBER

1623

DATE MAILED: 02/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/493,891	Applicant(s) LONGTON ET AL	
	Examiner Leigh C. Maier	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 November 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5-8,10-14 and 16-23 is/are pending in the application.
- 4a) Of the above claim(s) 10-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5-8 and 16-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

Claims 1, 2 and 16 have been amended. Claim 9 has been canceled. Claims 1-3, 4-8, 10-14 and 16-25 are pending. Claims 10-14 remain withdrawn as being drawn to a non-elected invention. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Any objection or rejection not expressly repeated has been withdrawn.

Claim Rejections - 35 USC § 112

Claims 1 and 16-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 is a product-by-process claim wherein the polysaccharide product is “free of residual conjugation activators and chemical promoters.” At page 5, 2nd full paragraph, the specification gives some examples of such “activators” and “promoters,” but does not clearly describe the full range of what is to be excluded from the products set forth in claims 16-22. Thus, the examiner maintains that one of ordinary skill would not be apprised of the metes and bounds of the claims. Claim 1 has been amended to include this limitation and is thereby included in this rejection.

Applicant’s arguments filed November 18, 2005 have been fully considered but they are not persuasive.

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Applicant cites a case wherein the limitation “said homopolymer being free from the [listed components] present in Hevea rubber.” The examiner agrees that such a limitation would be definite. One of ordinary skill can determine exactly what components are comprised in Hevea rubber, but it is not clear what the scope of “activators” and “promoters” is.

Claim Rejections - 35 USC § 102

Claims 16 and 17 are again rejected under 35 U.S.C. 102(a) as being anticipated by MARTEY et al (CAPLUS abstract 1998:529836, 1998), as set forth in the previous Office action.

Applicant's arguments filed November 18, 2005 have been fully considered but they are not persuasive. Applicant argues that the reference is not by “others” because the authors are also inventors on the present application. The examiner maintains that this reference is indeed by “others” because the two authors on the reference comprise an inventive entity that is different from that of the instant application.

Claim Rejections - 35 USC § 103

Claims 1-3, 5, 6, 16, and 17 are again rejected under 35 U.S.C. 103(a) as being unpatentable over HEINDEL et al (Bioconjugate Chem., 1994) in view of DIENER et al (US 4,415,552) and further in view of either of (1) AKANUMA et al (J. Biochem., 1978) or (2) MARTEY et al (CAPLUS abstract 1998:529836, 1998), as set forth in the previous Office action.

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Applicant's arguments filed November 18, 2005 have been fully considered but they are not persuasive.

Applicant first contends that MARTEY is not a proper reference. The examiner respectfully disagrees. This is addressed above.

Applicant further argues that HEINDEL does not teach the recited process for the polysaccharides set forth in claim 3. This was noted in the Office action.

Applicant objects to the use of DIENER because the reference "requires the use of a **water-soluble polysaccharide**, in contrast to the claimed method which employs an insoluble suspension of the polysaccharide in a non-reacting solvent." (emphasis in original) First of all, the examiner does not find the limitation requiring a suspension. It is further noted that the polysaccharides recited in claim 3 are water-soluble polysaccharides. Finally, Applicant contends that the reference does not teach the preparation of lactones. The examiner agrees. As was clearly stated in the previous Office action, it is HEINDEL that teaches the preparation of lactones.

Applicant contends that AKANUMA does not teach the lactonization process. Again, HEINDEL teaches the process. Further regarding this reference, Applicant states, "simply being able to prepare [CM-cellulose lactone] does not provide motivation to modify Heindel to achieve the method of Claim 3." The examiner agrees. However, this was not the reasoning used in the previous Office action. As discussed previously, it would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare CM-cellulose lactone by the method of HEINDEL for the art-disclosed utility. One of ordinary skill would be motivated to use this method to avoid the disadvantages of using chemical activators, as discussed in

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HEINDEL. Both AKANUMA and MARTEY disclose the CM-cellulose lactone, so one of ordinary skill would know that it is possible to prepare polysaccharide lactones. Therefore, the artisan would reasonably expect success in using the HEINDEL process to prepare this product. It would be further obvious to prepare the product having a degree of substitution as set forth in claims 1 and 2 because DIENER had taught that this molecular weight was useful in preparing allergen-CMC conjugates. It is DIENER that provides the motivation for the modification. AKANUMA merely provides additional evidence to support a reasonable expectation of success.

Applicant further contends that the combination of references do not teach all the claim limitations. However, Applicant fails to identify the omitted limitation(s).

The last paragraph at page 14 of Applicant's response reiterates the foregoing piecemeal analysis of the rejection. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). This applies to the rejections set forth hereinbelow, which Applicant similarly addresses in piecemeal fashion.

Claims 3, 5, 16, 20, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over HEINDEL et al (Bioconjugate Chem., 1994) in view of WEINSHENKER (US 5,068,227) and further in view of either of (1) AKANUMA et al (J. Biochem., 1978) or (2) MARTEY et al (CAPLUS abstract 1998:529836, 1998).

Applicant's arguments filed November 18, 2005 have been fully considered but they are not persuasive.

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Applicant first contends that MARTEY is not a proper reference. The examiner respectfully disagrees. This is addressed above.

Applicant argues that WEINSHENKER does not prepare lactones. Again, there was no statement in the previous Office action that the reference does prepare lactones. It is HEINDEL that teaches lactonization of polysaccharides to provide and activated species having utility as an intermediate for conjugation of other molecules. Applicant further objects to the reference because of the ultimate products formed when molecules are coupled to the cyclodextrin are allegedly different than what Applicant proposes to prepare. However, this is not particularly relevant to the rejection because it is only lactone products that are claimed and not the ultimate bioconjugates.

Applicant further contends that the combination of references do not teach all the claim limitations. However, Applicant fails to identify the omitted limitation(s).

Applicant further contends that there is no motivation to combine the references to achieve the claimed products. The motivation was clearly stated in the previous Office action. It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare CM-cyclodextrin lactone by the method of HEINDEL for the art-disclosed utility for the advantages discussed previously. Cyclodextrin is a 1,4-linked polysaccharide, so a CM substituent at position 2 or 3 would be expected to lactonize under these conditions, similar to CM-cellulose. Therefore, the artisan would reasonably expect success in using the HEINDEL process to prepare this product.

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Claims 3, 5, 16, 21, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over HEINDEL et al (Bioconjugate Chem., 1994) in view of ELSON (US 5,888,988) and further in view of either of (1) AKANUMA et al (J. Biochem., 1978) or (2) MARTEY et al (CAPLUS abstract 1998:529836, 1998).

Applicant's arguments filed November 18, 2005 have been fully considered but they are not persuasive.

Applicant first contends that MARTEY is not a proper reference. The examiner respectfully disagrees. This is addressed above.

Applicant argues that ELSON does not prepare lactones. Again, there was no statement in the previous Office action that the reference does prepare lactones. It is HEINDEL that teaches lactonization of polysaccharides to provide and activated species having utility as an intermediate for conjugation of other molecules as an intermediate for conjugation of other molecules as an alternative to the use of chemical coupling agents as used in ELSON.

Applicant further contends that the combination of references do not teach all the claim limitations. However, Applicant fails to identify the omitted limitation(s).

Applicant further contends that there is no motivation to combine the references to achieve the claimed products. The motivation was clearly stated in the previous Office action. It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare CM-chitosan lactone by the method of HEINDEL for the art-disclosed utility for the advantages discussed previously. Cyclodextrin is a 1,4-linked polysaccharide, so a CM substituent at position 2 (N) would be expected to lactonize under these conditions, similar to

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CMC. Therefore, the artisan would reasonably expect success in using the HEINDEL process to prepare this product.

Claims 3, 5, 8, 16, 19, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over HEINDEL et al (Bioconjugate Chem., 1994) in view of HATTORI et al (J. Agric. Food Chem., 1995) and further in view of either of (1) AKANUMA et al (J. Biochem., 1978) or (2) MARTEY et al (CAPLUS abstract 1998:529836, 1998).

Applicant's arguments filed November 18, 2005 have been fully considered but they are not persuasive.

Applicant first contends that MARTEY is not a proper reference. The examiner respectfully disagrees. This is addressed above.

Applicant argues that HATTORI does not prepare lactones. Again, there was no statement in the previous Office action that the reference does prepare lactones. It is HEINDEL that teaches lactonization of polysaccharides to provide and activated species having utility as an intermediate for conjugation of other molecules as an alternative to the use of chemical coupling agents as used in HATTORI.

Applicant further contends that one of ordinary skill would not have anticipated that CM-starch would survive the thermal conditions as claimed. However, Applicant presents no evidence to support this position. Applicant further contends that the combination of references do not teach all the claim limitations. However, Applicant fails to identify the omitted limitation(s).

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Applicant further argues that the references teach away from the invention because “applicant’s claimed process at a higher temperature was contrary to accepted wisdom because the prior art as a whole suggested using lower temperatures for optimum results.” Again, Applicant presents no evidence supporting this position. Furthermore, the examiner finds no particular temperature limitation in the claims.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare CM-starch lactone by the method of HEINDEL as an activated species to prepare the starch/protein conjugate and avoid the disadvantages of a carbodiimide coupling. Starch is a 1,4-linked polysaccharide, so a CM substituent at position 2 or 3 would be expected to lactonize under these conditions, similar to CMC. Therefore, the artisan would reasonably expect success in using the HEINDEL process to prepare this product. It would be further obvious to select any of the solvents taught by HEINDEL. Applicant has not demonstrated any criticality in any particular polysaccharide/solvent pair.

Claims 3, 5, 7, 9, 16, 18, 22, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over HEINDEL et al (Bioconjugate Chem., 1994) in view of MILL et al (US 4,003,972) and further in view of STREITWIESER et al (Introduction to Organic Chemistry, 1976).

Applicant’s arguments filed November 18, 2005 have been fully considered but they are not persuasive.

Applicant argues that MILL does not prepare lactones. Again, there was no statement in the previous Office action that the reference does prepare lactones. It is HEINDEL that teaches

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lactonization of polysaccharides to provide an activated species having utility as an intermediate for conjugation of other molecules as an alternative to the use of chemical coupling agents as used in MILL.

Applicant notes that MILL teaches that the methods described in the reference “have the advantage that they can be carried out in **aqueous solution at relative low temperatures.**” (emphasis in original) However, the HEINDEL method has the advantage of not introducing coupling agents into the mix. The fact that neither process incorporates every feature that might be desirable to one having ordinary skill further supports the examiner’s position that it would be within the scope of the artisan to select either method, including the one of HEINDEL.

STREITWIESER teaches that lactone formation is particularly favored when it results in a 5- or 6-membered ring, as discussed in the previous Office action. The examiner is attaching a copy of this evidentiary reference to complete the record as Applicant notes that it was unavailable.

The examiner maintains that it would have been obvious to one having ordinary skill in the art at the time the invention was made to use the process of HEINDEL to prepare lactones of the acidic polysaccharides taught by MILL, the ones specifically cited or similar ones, such as carboxy-starch, for the advantages discussed above. The artisan would be motivated to prepare a lactone as an active species to prepare conjugates taught in the reference. One of ordinary skill would reasonably expect success in the preparation of a lactone with these polysaccharides because the reaction of the acid at position 6 and the hydroxyl at position 3 would result in a 5-membered ring. It would be obvious to one of ordinary skill to select any of the solvents

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disclosed for the process. Applicant has not demonstrated any criticality in any particular polysaccharide/solvent pair.

Applicant's amendment necessitated the new ground of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Anna Jiang (571) 272-0627, may be contacted. The fax number for Group 1600, Art Unit 1623 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished application is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov> Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

Leigh C. Maier

Leigh C. Maier
Primary Examiner
February 2, 2006